

FIG. 1A-1

	Signal peptide	
MMP-1	MHSEPPLLLLFWG-----VVSHSEP-----ATLETQ	
MMP-2	MEALMARGALTGPLRALCLLGCLLSHAA-----AP-----SPIIKFPG	
MMP-3	MKSLPILLLLCVAV-----CSAYP-----LDGAARGE	
MMP-7	MR-LTVLCVAVCLL-----PGSLALP-----LPQE	
MMP-8	MSLKTLPFLLLLH-----VQISKAFP-----VSSK	
MMP-9	MSLWQPLVLLVVGCC-----FAAPRQRQSTLVLFPG	
MMP-10	MMHLAFVLLCLPV-----CSAYP-----LSGAAKEE	
MMP-11	MAPAAWLRSAARALLPPMLLLQLPPPLARALP-----	
MMP-12	MKFLILLLQ-ATA-----SGALP-----LNSSTSLE	
MT-MMP-1	MSPAPRPSRCLLPLLTGLTALASLGSAQSSSESP-----	
MT-MMP-3	MILLTFSTGRRLDFVH-----HSGVFFLQTLWLILCATVCG	
Consensus	M..L..L...L..-----...A.P-----.....	
	Pro-peptide	
MMP-1	DAETLKVMKQPRCGVPDVAQ-----FVLTEGNPRWEQTHLT	
MMP-2	DQNTIETMRKPRCGNPDVAN-----YNFFPRKP KWDKNQIT	
MMP-3	DSDTLEVMRKPRCGVPDVGH-----FRTFPGIP KWRKTHLT	
MMP-7	NSRVIEIMQKPRCGVPDVAE-----YSLFPNSPKWTSKVVT	
MMP-8	NEETLDMKKKPRCGVPDSSG-----FMLTPGNPKWERTNLT	
MMP-9	DSATLKAMRTPRCGVPLDGR-----FQTFEGDLKWHHHNIT	
MMP-10	DTDITLEVMRKPRCGVPDVGH-----ESSFPGMPKWRKTHLT	
MMP-11	APRPASSLRPPRCGVDPDPSD-GLSARNRQKREVLSSG--RWEKTDLT	
MMP-12	DTSTLEMMHAPRCGVPLDLH-----FREMPGGPVWRKHYIT	
MT-MMP-1	DADTMKAMRRPRCGVPDKFGAEIKANVRRKRYAIQ-G-LKWQHNEIT	
MT-MMP-3	DRNTIDWMKKKPRCGVPDQTRGSSKFHIRRKRYALTQ--KWQHKHIT	
Consensus	D..TL..MRKPRCGVPD...-----F...PG.PKW.....T	↑ IS-1

FIG. 1A-2

Pro-peptide

EQDVLVQKYLEKYNNLKNDRQVEKRRNSGPVV-EKLKQMQUEFFGLKVTGKP 79
 DVAPK-TDKELAVQYLNTF-YGCPKE-SCNLFVLKDTLKKMQKFFGLPQTGDL 89
 DTSMLVQKYLENYDLKDVVKQFVRRKDSGPVV-KKIREMQKFFGLGLEVTKGL 79
 AGMSELQWEQAQDY-LKRFYLYDSETKNANSLE-AKLKEMQKFFGLPITGML 74
 EKNTKTVQDYLEKFYQLPSNQYQSTR-KNGTNVIVEKLEKEMQKFFGLNVTGKP 78
 DLRTNLTDRQLAEELYRYGYTRVAEMRGESKSLGPALLLQKQLSLPETGEL 86
 DSNKDLAQYLEKYNNLEKDVKQFRRK-DSNLIV-KKIQGMQKFFGLGLEVTKGL 78
 -----PDVHHLHAERRGPQ-----PWHALPSSPAPATQE 67
 KNNVLFGERYLEKFYGLEINKLPVTMKYSGNLMKEKIQEMQHFLGLKVTGQL 79
 -----EAWLQQYGYLPPGDLRTHTQRSQSLS-AAIAAMQKFFGLQVTGKA 80
 TEQYFNVEVWLQKYGYLPPPTSPRMSVVRSAETMQ-SALAAAMQQFYGINMTGKV 88
L...Y.L.....-KL..MQKF.GL.VTGKL 100

Catalytic

YRIENYTPDLPRADVDAIEKAFQLWSNVTPLTFTKV-----SEQQADIM 160
 YRIIGYTPDLDPETVDDAFARAFQVWSDVTPLRFSRI-----HDGEADIM 170
 YRIVNYTPDLPKDAVDSAVEKALKVWEEVTPLTFSRL-----YEGEADIM 160
 YRIVSYTRDLPHITVDRLVSKALNMWGKEIPLHFRKV-----VWGTADIM 155
 YRIRNYTPQLSEAEVERAIKDAFELWSVASPLIFTRI-----SQGEADIN 159
 YWIONYSEDLPRAVIDDAFARAFALWSAVTPLTFTRV-----YSRDADIV 167
 YRIVNYTPDLPRDAVDSAIEKALKVWEEVTPLTFSRL-----YEGEADIM 159
 YRILRFPWQLVQEQVRQTMAEALKVWSDVTPLTFTTEV-----HEGRADIM 156
 YRINNYPDMNREDVDYAIRKAFQVWSNVTPPLKFSKI-----NTGMADIL 160
 FCIONYTPKVGEYATYEAIRKAFRVWESATPLRFREVVPYAIREGHEKQADIM 178
 YSINKNVTPKVGDPETRKAIIRRAFQVWQNVTPLTFTFEVVPYSELENGK-RDVDIP 185
 YRI.NYTPDL...VD.AI.KAF.VWS.VTPLTF..V-----G.ADIM 200

↑ IS-2

FIG. 1B-1

	Catalytic	Catalytic
MMP-1	ISFVRGDRDNSPFDGPGGNLAHAFQPGPGIGGDAHFDEHERWTN-NFTEYN	YGFPCHEALFTMGNAEQPCKPFRFQGTSDSCTTEGRTDGYRWCCTED
MMP-2	INFGRWEHGDGYPFDGKDLLAHAFAPGTGVGDSHFDDDELWTLGEGQVVR	-----
MMP-3	ISFAVREHGDFYPFDGPGNVLAHAYAPGPGINGDAHFDDDEQWTK-DTTGTN	-----
MMP-7	IGFARGAHGDSYPFDGPGNTLAHAFAPGTGLGDAHFDEDERWTDGSSLGIN	-----
MMP-8	IAFYQRDHGDNSPFDGPGNLAHAFQPGQIGGDAHFDAEETWTN-TSANYN	FGFCPSERLYTRDGNADGKPCQPFIFQQQSYSACTDGRSDGYRWCATTAN
MMP-9	IQFGVAEHGDDGYPFDGKDLLAHAFPPGPGIQGDAHFDDDELWSLGKGVVVP	-----
MMP-10	ISFAVKEHGDFYSFDGPGHSLAHAYPPGPGLYGDIHFDDDEKWT-E-DASGTN	-----
MMP-11	IDFARYWDGDDLFPFDGPGILAHAFPPKTHREGDVHFYDETWIGDDQGTD	-----
MMP-12	VVFARGAHGDFHAFDGKGGILAHAFPGSGIGGDAHFDEDEFWTT-HSGGTN	-----
MT-MMP-1	IFFAEGFHGDSPTFDGEGGFLAHAYFPNIGGDTHFDSAEPTV-RNEDLN	-----
MT-MMP-3	IIFASGFHGDSSPFDGEGGFLAHAYFPNIGGDTHFDSDEPWTGLNPNHGDG	-----
Consensus	I.FA...HGD...PFDGPGG.LAHAF.PGPGIGGDAHFD.DE.WT.-.....N	-----
MMP-1		-----
MMP-2		-----
MMP-3		-----
MMP-7		-----
MMP-8		-----
MMP-9		-----
MMP-10		-----
MMP-11		-----
MMP-12		-----
MT-MMP-1		-----
MT-MMP-3		-----
Consensus		-----

FIG. IB-2

 VKYGNADGEYCKFPFLFNGKEYNSCTDTGRSDGFLWCSTTYNFEKDGK 211
 ----- 270
 ----- 211
 ----- 207
 ----- 210
 TRFGNADGAACHFPFIFEGRSYSACTTDGRSDGLPWCSTTANYDTDDR 267
 ----- 210
 ----- 208
 ----- 211
 ----- 229
 ----- 237
 ----- 300

 YDRDKKYGFCPETAMSTV-GGNSEGAPCVFPFTFLGNKYESCTSAGRS 211
 ----- 369
 ----- 211
 ----- 207
 ----- 210
 YDRDKLFGFCPTRADSTVMGGNSAGELCVFPFTFLGKEYSTCTSEGRG 367
 ----- 210
 ----- 208
 ----- 211
 ----- 229
 ----- 237
 ----- 400

FIG. 1C-1

	Catalytic	Hinge
MMP-1	-----LHRVAA-HELGHSLGLSHST	-----RSQNP
MMP-2	DGKMWCATTANYDDDRKWGFCPDQGYSLFLVAA-HEFGHAMGLEHSQ	-----ASPDIDLGTG
MMP-3	-----LFLVAA-HEIGHSLGLFHS	-----PPDSPETPLVPT
MMP-7	-----FLYAA-THLGHSLGMGHSS	-----LSSNP
MMP-8	-----LFLVAA-HEFGHSLGLAHSS	APPTVCPTGPPTVHPSERPTAGPTGPPSAGPTGPPTAGPSTA-TTVP
MMP-9	DGRLWCATTSNFSDSKKWGFCPDQGYSLFLVAA-HEFGHALGLDHSS	-----PPASTEELVPTK
MMP-10	-----LFLVAA-HELGHSLGLFHS	-----QPWPTVTSRTPALGPQAGIDTNE
MMP-11	-----LLQVAA-HEFGHVLGLQHTT	-----DPKENQRL
MMP-12	-----LFLTAV-HEIGHSLGLGHSS	-----GESGFTKMPPQPRTTSRPSVP
MT-MMP-1	-----GNDIFLVAV-HELGHALGLEHSS	-----SPDKIPPPTRLPTVPPHRSIPPADPRKNDPRKPPRPPT
MT-MMP-3	-----NDLFLVAV-HELGHALGLEHSN	-----
Consensus	-----LFLVAA-HE.GHSLGL.HS.	-----
MMP-1		
MMP-2		
MMP-3		
MMP-7		
MMP-8		
MMP-9		
MMP-10		
MMP-11		
MMP-12		
MT-MMP-1		
MT-MMP-3		
Consensus		

FIG. ID-1

	Hemopexin
MMP-1	FTSVFWPQLPngleAAyEFADrDEVrFFKGNKYWAV-QGQNVLHGYPKDIYSSFGFPR
MMP-2	LVATFwPElPEKIDAVyEAPQEEKAVFFAGNEyWIY-SASTLERGYPKPLTS-LGLPP
MMP-3	LISFwPSLPSGVDAAYEVTskDLVFIKGNQFWAI-RGNEVRAGYPRGIHT-LGFPP
MMP-7	-----
MMP-8	FISLFWPSLPTGIQAAYEDFDrdLlFLFKGNQYWAL-SGYDILQGYPKDISN-YGFPS
MMP-9	LIADKwPALPRKIDSVFEEPLSKKLFFFSGRQVWVYTgASVL--G-PRRLDK-LGLGA
MMP-10	LISAFwPSLPSYLDAAyEVNSrdTVFIKGNEFWAI-RGNEVQAGYPRGIHT-LGFPP
MMP-11	LASRHwQGLPSpVDAAFE-DAQGHlWFFQGAQYWVY-DGEKpVLG-PAPLTe-LGLVR
MMP-12	LISSLwPTLPSGIEAAyEIEARNQVFLFKDDKYWLI-SNLRPEPNYPKSIHS-FGFpN
MT-MMP-1	PIGQFWRGlpASINTAYERKDGKEVF-FKGDkHwVF-DEASLEPGYPKHike-LGRGL
MT-MMP-3	QITyFWRGlpPSIDAVyENSdGNFVF-FKGNKYWVF-KDTTLQPGYPHDlIT-LGSGI
Consensus	LIS.FWP.LP...DAAYE.....VF.FKGN.YW...-.....GYP..I...-LG.P.

	Hemopexin
MMP-1	MI AHDFPGIGHKVDAVFMKDGFF--YFFHGTRQYKfDEPKT-KRILTL-QKANS-WFNC
MMP-2	LIADAwNAIPDNLDaVVdLQGGHsYFFKGAyYlKlENQs-LKsvKF-GsIKSDWLGC
MMP-3	QIAEDFPGIDSKIDAVFEeFGFF--YFFTGSSQLEFDpNA-KKVThT-LKSNS-WLNC
MMP-7	-----
MMP-8	SISGAFFGIESKVDaVFQqEHFF--HVFSGPRYyAFDLIA-QRVTRV-ARGNK-WLNC
MMP-9	EVDRMFPGVPLDTHdVfQYREKA--YFCQDRFYWRvSSrSELNQVDQVGyVtYdILQC
MMP-10	LIADDFPGVEPKVDaVLQAFGFF--YFFSGSSQFEFDpNA-RMvThI-LKSNS-WLHC
MMP-11	R-ATDWRGVPSEIDAAfQDADGYA-YfLRGRlyWKfDEpVK-VKALEGFpRLVGPdFFG
MMP-12	LI TKNFQGIgPKIDAVfYSKNKY-YyFFQGSNQfEYdELL-QRITKT-LKSNS-WFGC
MT-MMP-1	NIKVWE-GIPESPRGSFMGSDEvFTYfYKGNKYWkFNnQKLKVEPGYPKsALRDwMGC
MT-MMP-3	PITVWK-GIPESpQAFVHKENGFTYfYKEGVLEIQITrySRLEPGHPRsILKDLSGC
Consensus	.I...F.GI....DAVF.....--YFF.G.....FD...-.....-W...C

FIG. ID-2

TVKHIDAA-LSEENTGKTYFFVANKYWRYDEYKRSMDPGYPK	413
DVQRVDAA-FNWSKNKTTYIFAGDKFWRYNVKKKMDPGFPK	604
TVRKIDAA-ISDKEKNKTYFFVEDKYWRFEDEKRNSMEPGFPK	424
-----	267
SVQAIDAA-VFYRS--KTYFFVNDQFWRYDNQRQFMEPGYPK	411
DVAQVTGA-LRSGR-GKMLLESGRRLLWRFEDVKAQMVDPRSAS	648
TIRKIDAA-VSDKEKKKTYFFAADKYWRFEDENSQSMEQGFPR	423
FP--VHAALVWGPEKNKIYFFRGRDYWRFHPSSTRRVDSPVPR	424
FVKKIDAA-VFNPRFYRTYFFVDNQYWRYDERRRQMMDPGYPK	416
PTDKIDAA-LFWMPNGKTYFFRGNKYRNFNEELRAVDSEYPK	451
PPHGIDSA-IWVEDVGKTYFFKGDYRWRYSEEMKTMDPGYPK	472
.V..IDAA-.....KTYFF....YWR.DE....MDPG.PK	700

RKN-----	469
-----	660
-----	477
-----	267
RYG-----	467
PED-----	707
-----	476
CAEPANTFL-----	488
-----	470
PSGGRPDEGTEETE-VIIIEVDEEGGAVSAAAVLPVLLL	549
DGPTDRVKEGHSPPDDVDIVIKLDNTASTVKAIAIVIPCILA	571
-----	800

FIG. 1E

MMP-1	----	469
MMP-2	----	660
MMP-3	----	477
MMP-7	----	267
MMP-8	----	468
MMP-9	----	708
MMP-10	----	476
MMP-11	----	489
MMP-12	----	470
MT-MMP-1	LLVLAVGLAVFFRRHGTPTRRLLYCQRSLDKV	582
MT-MMP-3	LCLLVLVYTVFQFKRKGTPTRHILYCKRSMQEWV	604
Consensus	-----	833

FIG. 2

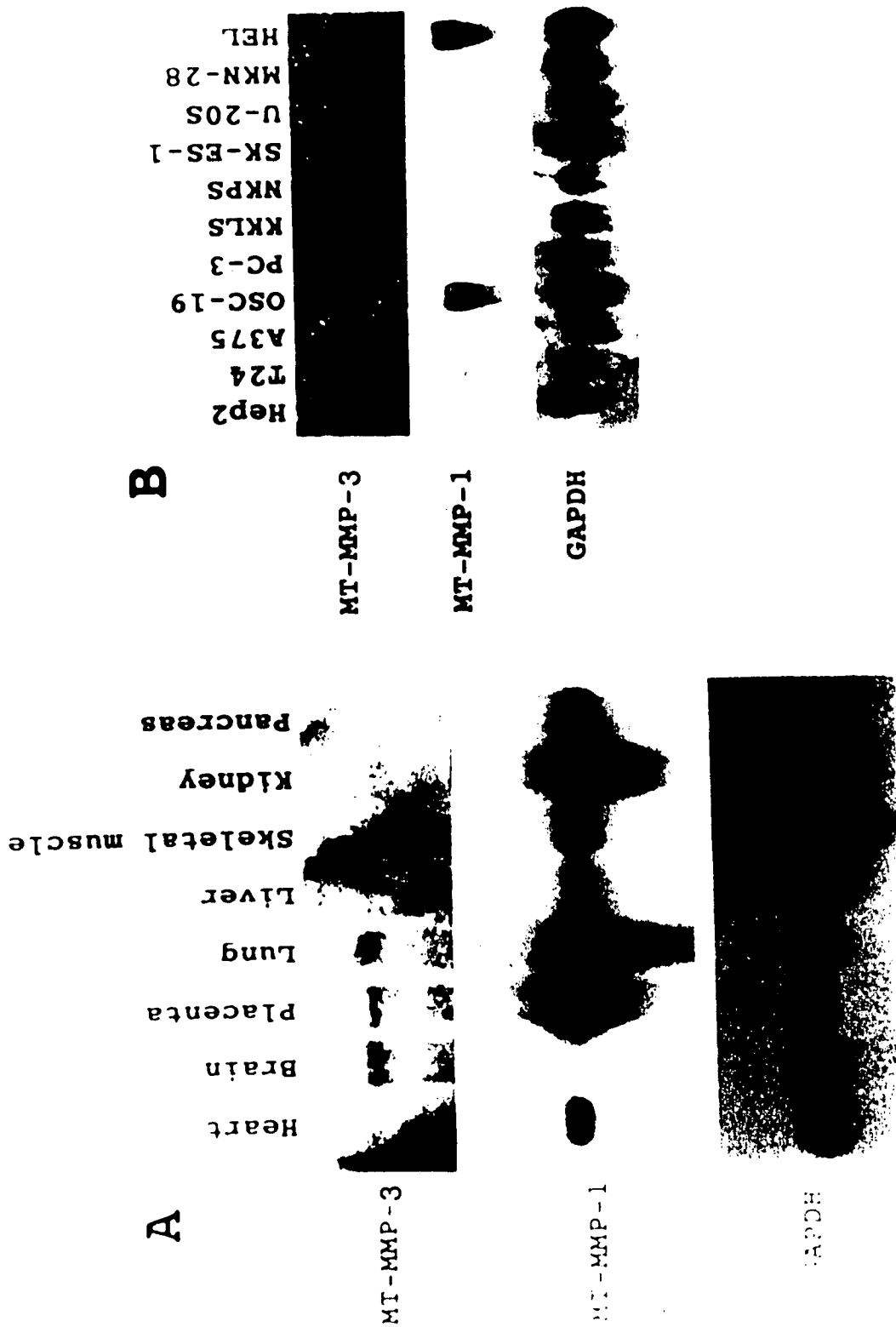
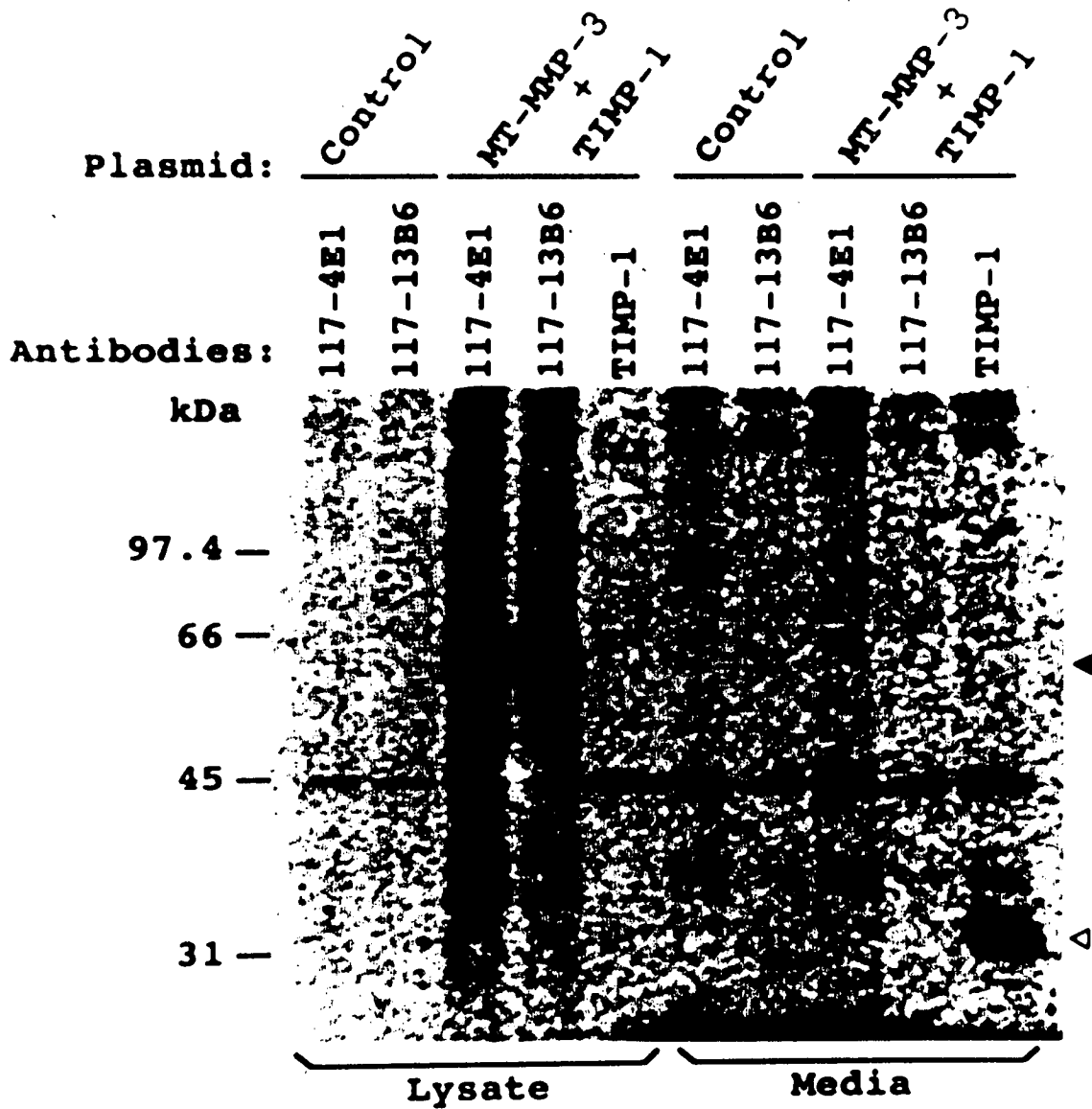


FIG. 3



002727" 2004E260

FIG. 4

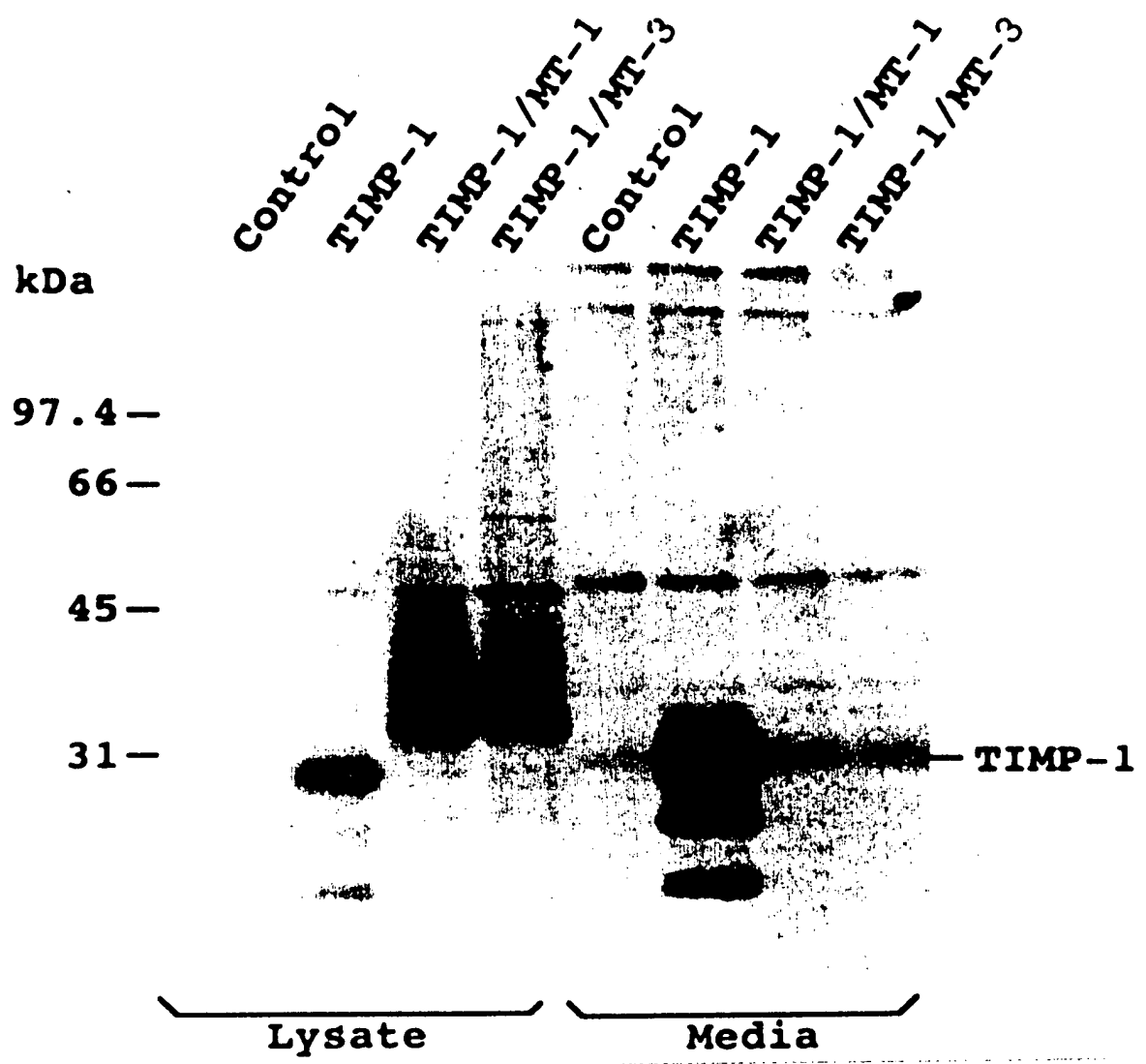
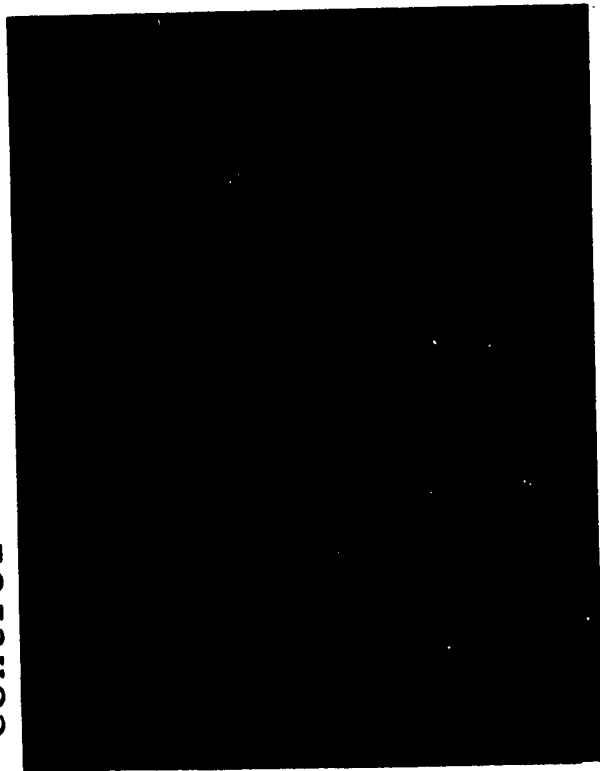


FIG. 5

Control



TIMP-1/MT-3



FIG. 6

